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NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	DEC 01	ChemPort single article sales feature unavailable
NEWS	3	JUN 01	CAS REGISTRY Source of Registration (SR) searching enhanced on STN
NEWS	4	JUN 26	NUTRACEUT and PHARMAML no longer updated
NEWS	5	JUN 29	IMSCOPROFILE now reloaded monthly
NEWS	6	JUN 29	EPFULL adds Simultaneous Left and Right Truncation (SLART) to AB, MCLM, and TI fields
NEWS	7	JUL 09	PATDPAFULL adds Simultaneous Left and Right Truncation (SLART) to AB, CLM, MCLM, and TI fields
NEWS	8	JUL 14	USGENE enhances coverage of patent sequence location (PSL) data
NEWS	9	JUL 27	CA/CAplus enhanced with new citing references
NEWS	10	JUL 16	GBFULL adds patent backfile data to 1855
NEWS	11	JUL 21	USGENE adds bibliographic and sequence information
NEWS	12	JUL 28	EPFULL adds first-page images and applicant-cited references
NEWS	13	JUL 28	INPADOCDB and INPAFAMDB add Russian legal status data
NEWS	14	AUG 10	Time limit for inactive STN sessions doubles to 40 minutes
NEWS	15	AUG 18	COMPENDEX indexing changed for the Corporate Source (CS) field
NEWS	16	AUG 24	ENCOMPLIT/ENCOMPLIT2 reloaded and enhanced
NEWS	17	AUG 24	CA/CAplus enhanced with legal status information for U.S. patents
NEWS	18	SEP 09	50 Millionth Unique Chemical Substance Recorded in CAS REGISTRY
NEWS	19	SEP 11	WPIDS, WPINDEX, and WPIX now include Japanese FTERM thesaurus

NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4,
AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009.

NEWS HOURS STN Operating Hours Plus Help Desk Availability
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Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 21:42:11 ON 13 SEP 2009

=> file reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.66       0.66

FILE 'REGISTRY' ENTERED AT 21:44:07 ON 13 SEP 2009
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STRUCTURE FILE UPDATES:   11 SEP 2009  HIGHEST RN 1182870-06-9
DICTIONARY FILE UPDATES:  11 SEP 2009  HIGHEST RN 1182870-06-9

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TSCA INFORMATION NOW CURRENT THROUGH June 26, 2009.

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  conducting SmartSELECT searches.

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predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> s safinamide
L1            2 SAFINAMIDE

=> d l1 1-2

L1   ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   202825-46-5  REGISTRY
ED   Entered STN:  19 Mar 1998
CN   Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)-,
     methanesulfonate (1:1)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)-,
     monomethanesulfonate (9CI)
CN   Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (S)-,
     monomethanesulfonate
OTHER NAMES:
CN   (S)-2-[[4-[(3-Fluorobenzyl)oxy]benzyl]amino]propanamide methanesulfonate
CN   NW 1015
CN   PNU 151774E
CN   Safinamide mesylate
FS   STEREOSEARCH
MF   C17 H19 F N2 O2 . C H4 O3 S
SR   CA
LC   STN Files:   ADISINSIGHT, BIOSIS, CA, CAPLUS, CHEMCATS, EMBASE,
       IMSPATENTS, IMSRESEARCH, IPA, MRCK*, PROUSDDR, TOXCENTER, USPATFULL
         (*File contains numerically searchable property data)

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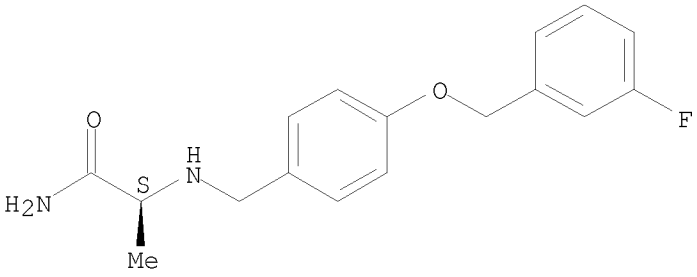
CRN 133865-89-1
CMF C17 H19 F N2 O2

Absolute stereochemistry. Rotation (+).



CM 2

CRN 75-75-2
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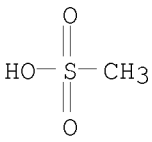
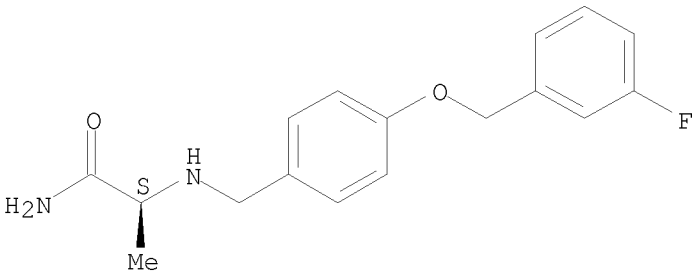


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

25 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
25 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2009 ACS on STN
RN 133865-89-1 REGISTRY
ED Entered STN: 17 May 1991
CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)-
(CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (S)-
OTHER NAMES:
CN (S)-2-[[4-[(3-Fluorobenzyl)oxy]benzyl]amino]propanamide
CN FCE 26743
CN Safinamide
FS STEREOSEARCH
MF C17 H19 F N2 O2
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, BIOSIS, CA, CAPLUS, CASREACT, CBNB,
CHEMCATS, CIN, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS,
IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, RTECS*,
TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

50 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
50 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	9.93	10.59

FILE 'CAPLUS' ENTERED AT 21:44:49 ON 13 SEP 2009
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FILE COVERS 1907 - 13 Sep 2009 VOL 151 ISS 12
FILE LAST UPDATED: 11 Sep 2009 (20090911/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2009

CAplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2009.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate substance identification.

The ALL, BIB, MAX, and STD display formats in the CA/CAplus family of databases have been updated to include new citing references information. This enhancement may impact record import into database management software. For additional information, refer

to NEWS 9.

=> s l1
L2 68 L1

=> s l2 and parkinson
31378 PARKINSON
L3 25 L2 AND PARKINSON

=> d l3 1-25 ibib abs hitstr

L3 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2009:740263 CAPLUS
DOCUMENT NUMBER: 151:33925
TITLE: Process for the production of 2-[4-(3- and 2-fluorobenzyloxy) benzylamino]propanamides
INVENTOR(S): Barbanti, Elena; Caccia, Carla; Salvati, Patricia; Velardi, Francesco; Ruffilli, Tiziano; Bogogna, Luigi
PATENT ASSIGNEE(S): Newron Pharmaceuticals S.p.A., Italy
SOURCE: U.S. Pat. Appl. Publ., 27pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20090156678	A1	20090618	US 2008-338825	20081218
WO 2007147491	A1	20071227	WO 2007-EP5105	20070608

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2006-12565 A 20060619
WO 2007-EP5105 A2 20070608
OTHER SOURCE(S): CASREACT 151:33925; MARPAT 151:33925

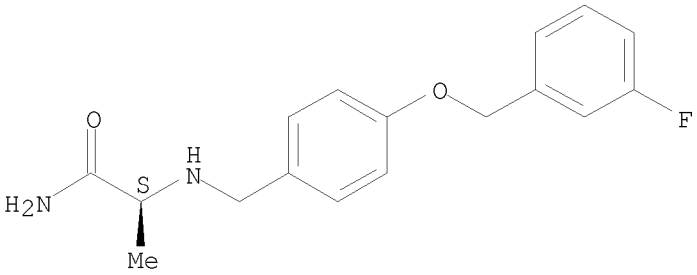
AB There is disclosed a process for obtaining therapeutically active 2-[4-[3- and 2-(fluorobenzyloxy)benzyl]amino]propanamides (safinamide and ralfinamide) and their salts with pharmaceutically acceptable acids with high purity, in particular, with a content of dibenzyl derivs. impurities lower than 0.03%, preferably lower than 0.01% by weight The process is carried out by submitting the Schiff bases intermediates 2-[4-(3- and 2-fluorobenzyloxy)benzylideneamino]propanamides to catalytic hydrogenation in the presence of a heterogeneous catalyst in a protic organic solvent. This process provides safinamide and ralfinamide having reduced in the content of impurities, i.e. (S)-2-[[3-(2-Fluorobenzyl)-4-[(2-fluorobenzyl)oxy]benzyl]amino]propanamide or (S)-2-[[3-(3-Fluorobenzyl)-4-[(3-fluorobenzyl)oxy]benzyl]amino]propanamide at lower than 0.01 weight%. Thus, an autoclave was loaded with 4-(2-fluorobenzyloxy)benzaldehyde (2.0 kg, 8.69 mol), followed by adding a solution of L-alaninamide hydrochloride (1.2 kg, 9.63 mol) and triethylamine (0.97 kg, 9.63 mol) in methanol (9.5 kg). The mixture was stirred at 20-25° for about 1 h and then, after seeding it with a few grams of

(S)-2-[4-(2-fluorobenzyloxy)benzylideneamino]propanamide, the stirring is continued for addnl. 15 min. To the stirred heterogeneous mixture, methanol (1.6 kg) and wet (50% H2O) Pt/C 5% (0.28 kg) were then added at 20-25°. The air was purged from the autoclave with nitrogen and then hydrogen was introduced at 5.0 bar. The reaction mixture was hydrogenated at the pressure of 5.0 bar and temperature of 30-35° for 5 h, cooled to 15° and, after addition of methanol (4.8 kg) and heating to 40-45°, was filtered. The solid was washed with methanol (1.6 kg). The solvent was removed from the combined filtrate under reduced pressure at about 30° and the residue was treated with water (5 L) at 20-25° on cooling and under stirring. The heterogeneous mixture was further cooled to 15-20°, kept at this temperature for 1 h, and then filtered. The collected solid was washed with cool water (4 L) and dried under reduced pressure to give 2.23 kg (85.0% yield) of (S)-2-[4-(2-fluorobenzyloxy)benzylamino]propanamide (ralfinamide) with a HPLC purity of 98.8 (area %) and a C,O-dialkylated product, (S)-2-[3-(2-fluorobenzyl)-4-(2-fluorobenzyloxy)benzylamino]propanamide content of 0.01% by weight

IT 133865-89-1P, (S)-2-[[4-[(3-Fluorobenzyl)oxy]benzyl]amino]propanamide 202825-46-5P, (S)-2-[[4-[(3-Fluorobenzyl)oxy]benzyl]amino]propanamide methanesulfonate
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-[4-(3- and 2-fluorobenzyloxy)benzylamino]propanamides by catalytic hydrogenation of 2-[4-(3- and 2-fluorobenzyloxy)benzylideneamino]propanamides (Schiff bases))

RN 133865-89-1 CAPLUS
CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

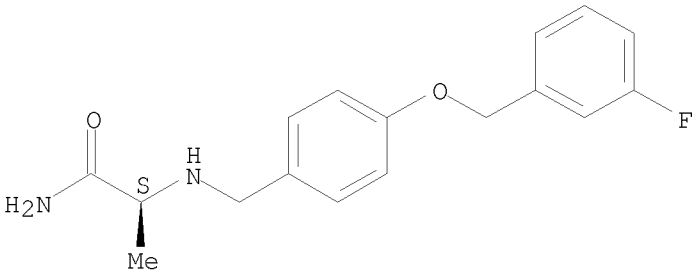


RN 202825-46-5 CAPLUS
CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

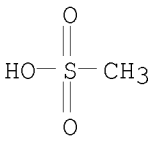
CRN 133865-89-1
CMF C17 H19 F N2 O2

Absolute stereochemistry. Rotation (+).



CM 2

CRN 75-75-2
CMF C H4 O3 S



L3 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2009:738936 CAPLUS
DOCUMENT NUMBER: 151:77763
TITLE: Process for the production of highly pure 2-[4-(3- or 2-fluorobenzyloxy)benzylamino]propanamides as cytochrome P450 inhibitors and their pharmaceutical compositions and use in the treatment of diseases
INVENTOR(S): Barbanti, Elena; Faravelli, Laura; Salvati, Patricia; Canevotti, Renato; Ponzini, Francesco
PATENT ASSIGNEE(S): Newron Pharmaceuticals S.p.A., Italy
SOURCE: PCT Int. Appl., 124pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009074478	A1	20090618	WO 2008-EP66559	20081201
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: EP 2007-23937 A 20071211
OTHER SOURCE(S): CASREACT 151:77763

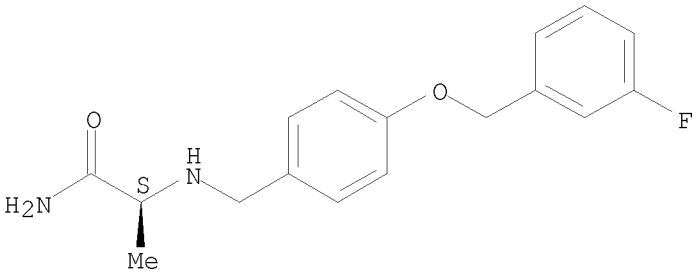
AB The invention relates to the process for obtaining therapeutically active [(fluorobenzyloxy)benzylamino]propanamides, and their salts with high purity. The title compds. were prepared via O-alkylation of 4-hydroxybenzaldehyde with benzyl halides; the resulting benzyloxybenzaldehydes underwent condensation with alaninamides to give the Schiff bases, which underwent reduction to give the title compds. All the invention compds. were evaluated for their cytochrome P 450 inhibitory activity.

IT 133865-89-1P
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(production of (benzylamino)propanamides as cytochrome P 450 inhibitors useful in the treatment of diseases via O-alkylation of hydroxybenzaldehyde with benzyl halides followed by reductive amination with alaninamides)

RN 133865-89-1 CAPLUS

CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 202825-46-5P
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(production of (benzylamino)propanamides as cytochrome P 450 inhibitors useful in the treatment of diseases via O-alkylation of hydroxybenzaldehyde with benzyl halides followed by reductive amination with alaninamides)

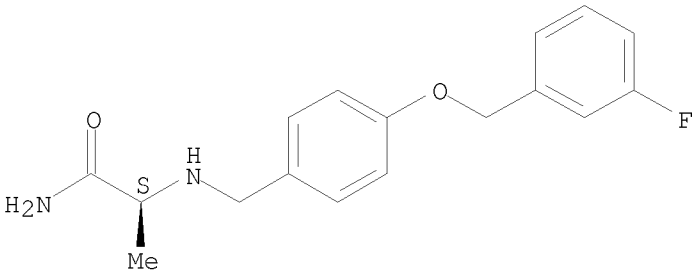
RN 202825-46-5 CAPLUS

CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 133865-89-1
CMF C17 H19 F N2 O2

Absolute stereochemistry. Rotation (+).



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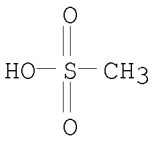


REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2009:523722 CAPLUS
DOCUMENT NUMBER: 150:487794
TITLE: AMPA receptor antagonists for Parkinson's disease and movement disorders
INVENTOR(S): Hanada, Takahisa; Hibi, Shigeki; Miyazaki, Kazuki
PATENT ASSIGNEE(S): Eisai R & D Management Co., Ltd., Japan
SOURCE: PCT Int. Appl., 62pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009054544	A1	20090430	WO 2008-JP69820	20081024

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2007-996078P P 20071026
OTHER SOURCE(S): MARPAT 150:487794
AB The invention provides methods for treating Parkinson's disease

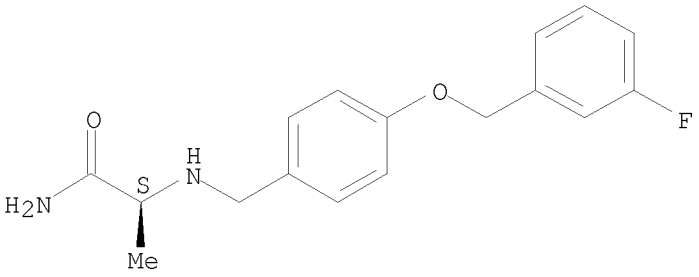
by administering to patients therapeutically effective amts. of AMPA receptor antagonists in combination with one or more other active ingredients useful for treating Parkinson's disease. The invention provides methods for treating movement disorders by administering to patients therapeutically effective amts. of AMPA receptor antagonists in optionally combination with one or more other active ingredients that are useful for treating movement disorders. The invention also provides pharmaceutical combinations, kits, and pharmaceutical compns. comprising therapeutically effective amts. of AMPA receptor antagonists, and optionally, one or more other active ingredients that are useful for treating Parkinson's disease and/or movement disorders.

IT 133865-89-1, Safinamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(AMPA receptor antagonists for Parkinson's disease and movement disorders)

RN 133865-89-1 CAPLUS

CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:1502800 CAPLUS

DOCUMENT NUMBER: 150:55709

TITLE: Preparation of substituted 2-[2-(phenyl)ethylamino]alkaneamide derivatives as sodium and/or calcium channel modulators

INVENTOR(S): Melloni, Piero; Restivo, Alessandra; Izzo, Emanuela; Francisconi, Simona; Colombo, Elena; Sabido-David, Cibele

PATENT ASSIGNEE(S): Newron Pharmaceuticals S.p.A., Italy

SOURCE: PCT Int. Appl., 88pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

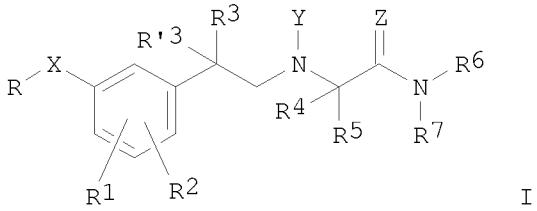
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008151702	A1	20081218	WO 2008-EP3848	20080514

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,

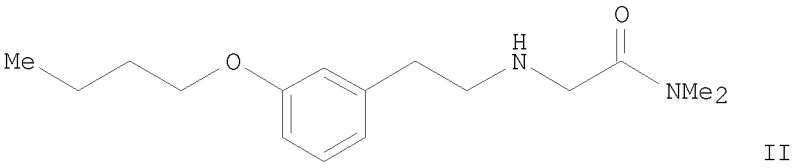
ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH,
PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,
IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2007-11766 A 20070615
OTHER SOURCE(S): MARPAT 150:55709

GI



I



II

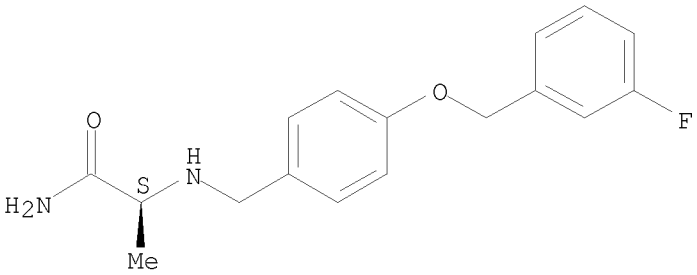
AB Title compds. I [X = O, S or SO2; Y = H, OH or O-alkyl; Z = O or S; R = alkyl; ω-trifluoroalkyl; R1 and R2 independently = H, OH, alkoxy, alkylthio, halo, CF3 or CH2CF3; R3 and R'3 independently = H or alkyl; R4 and R5 independently = H, alkyl; or R4 = H and R5 = CH2-OH, CH2-O-alkyl, CH(CH3)-OH, (CH2)2-S-CH3, benzyl or 4-hydroxybenzyl; or R4 and R5, taken together with the adjacent carbon atom, form a cycloalkyl; R6 and R7 independently = H or alkyl; or NR6R7 = 5- to 6-membered monocyclic saturated heterocycle; with the proviso], and their pharmaceutically acceptable salts, are prepared and disclosed. Thus, e.g., II was prepared by in 5 steps starting from 2-(3-benzyloxyphenyl)ethylamine hydrochloride. Selected I were tested in TTXs-sodium channel influx assay, e.g., II exhibited inhibition of Na+ influx channels with IC50 value of 1.5 μM. I and pharmaceutically acceptable salts thereof, pharmaceutical compns. containing them as active ingredient and their use as sodium and/or calcium channel modulators useful in preventing, alleviating and curing a wide range of pathologies, including, but not limited to, neurol., cognitive, psychiatric, inflammatory, urogenital and gastrointestinal diseases, where the above mechanisms have been described as playing a pathol. role.

IT 133865-89-1, Safinamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of substituted phenylethylaminoalkaneamide derivs. as sodium and/or calcium channel modulators)

RN 133865-89-1 CAPLUS

CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:1338451 CAPLUS
DOCUMENT NUMBER: 149:541636
TITLE: Combination pharmaceutical compositions comprising minicapsules or minispheres of, for example, nimodipine and tacrolimus
INVENTOR(S): Coulter, Ivan
PATENT ASSIGNEE(S): Sigmoid Pharma Ltd., Ire.
SOURCE: PCT Int. Appl., 109pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008132712	A2	20081106	WO 2008-IE53	20080501
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 2063875	A2	20090603	EP 2008-738144	20080501
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, AL, BA, MK, RS				

PRIORITY APPLN. INFO.: US 2007-924132P P 20070501
WO 2008-IE53 W 20080501

AB A modified release dosage product is provided, comprising a plurality of minicapsules or minispheres containing various active agents, for example, a calcium channel blocker, such as nimodipine, and/or a calcineurin inhibitor, such as tacrolimus. Uncoated minicapsules or minispheres encapsulating micronized nimodipine for immediate release and a controlled release polymer coated minicapsule or minisphere encapsulating micronized nimodipine for delayed, sustained, controlled or targeted release are described. Uncoated seamless minicapsules, the core of which comprise

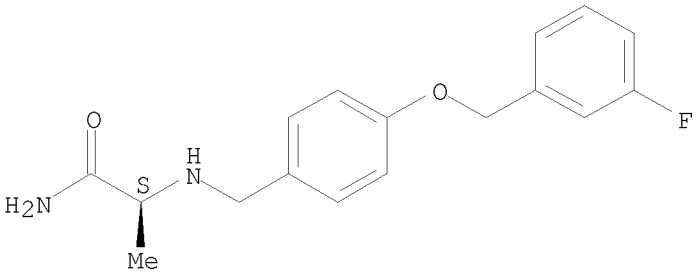
tacrolimus lipid-based formulation for immediate release and a controlled release polymer coated seamless minicapsule, the core of which comprises tacrolimus lipid-based formulation for delayed, sustained, controlled release or targeted release are also described. The final dosage form may be a hard gelatin capsule. Thus, nimodipine multiparticulate seamless minicapsules were produced containing nimodipine 37.5%, gelatin 56.3% and sorbitol 6.3%, and some of the minicapsules were coated with Surelease. Tacrolimus minicapsules were also produced comprising a core containing tacrolimus 3.25%, Labrafil 36.4%, olive oil 47.65%, and ethanol 12.7%, and a shell containing gelatin 90.0% and sorbitol 10.0%, and some of the minicapsules were first coated with Eudragit RS30D followed by Eudragit FS30D. The uncoated and coated nimodipine minicapsules and uncoated and coated tacrolimus minicapsules were blended into the final dosage form.

IT 133865-89-1, Safinamide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled-release compns. comprising combination of nimodipine and tacrolimus encapsulated in minicapsules or minispheres)

RN 133865-89-1 CAPLUS

CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L3 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:1202499 CAPLUS
DOCUMENT NUMBER: 150:320435
TITLE: New frontiers in the pharmacological management or Parkinson's
AUTHOR(S): Gottwald, Mildred D.; Aminoff, Michael J.
CORPORATE SOURCE: Jazz Pharmaceuticals, Inc., Palo Alto, CA, USA
SOURCE: Drugs of Today (2008), 44(7), 531-545
CODEN: MDACAP; ISSN: 1699-3993
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Rasagiline, a selective COMT inhibitor, and rotigotine, a transdermal dopamine (D2) agonist, are two new agents that have been approved in the U.S. and Europe for the treatment of Parkinson's disease. Rasagiline is approved in the U.S. for both monotherapy and as an adjunct to levodopa. Its role in preventing disease progression has yet to be proven, but a large-scale study (ADAGIO) is under way. Rotigotine is approved for early-stage disease in Europe and the U.S. but is only approved in Europe for late-stage disease. It has recently been recalled due to the formation of insol. crystals that interfere with absorption and may reduce its efficacy. Measures are being taken by the manufacturer to solve this problem. Istradefylline, and adenosine receptor antagonist, showed early promise but efficacy has not been demonstrated consistently, possibly due to higher than expected placebo effect. This has resulted in a nonapprovable letter from the FDA. With

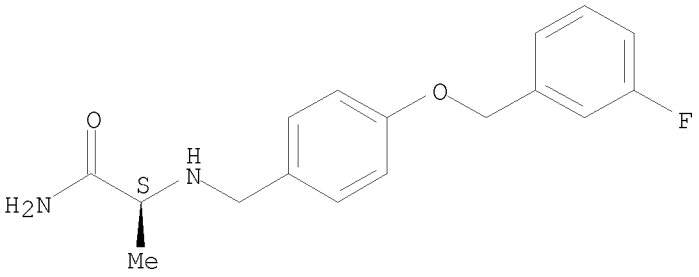
regard to perampanel, addnl. studies are needed to demonstrate safety and efficacy. Sanifamide and pardoprunox are agents that target multiple receptors that may modulate dyskinesia and other nonmotor symptoms in addition to motor symptoms, but phase III data are not yet available. Lusuride is an older dopamine agonist that has been reformulated as a transdermal patch and as a s.c. injection and may offer advantages in refractory patients with motor fluctuations. Sphermaine is a novel cell therapy designed to provide a localized source of levodopa directly to the brain. Gene therapies including AAV-GAD, AAV-AADC and AAV2-neurturin are in early stages of development in patients with advanced-stage disease but early safety data are promising.

IT 133865-89-1, Safinamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(safinamide targeted multiple receptors and may modulate dyskinesia, motor and non-motor symptoms in patient with Parkinson's disease)

RN 133865-89-1 CAPLUS

CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:718592 CAPLUS

DOCUMENT NUMBER: 149:69382

TITLE: An expert opinion on safinamide in Parkinson 's disease

AUTHOR(S): Onofrj, Marco; Bonanni, Laura; Thomas, Astrid

CORPORATE SOURCE: Department of Oncology and Neuroscience, Ageing Research Center, CeSI, University G D'Annunzio of Chieti-Pescara, University Foundation 'G D'Annunzio', Chieti-Scalo, 66013, Italy

SOURCE: Expert Opinion on Investigational Drugs (2008), 17(7), 1115-1125
CODEN: EOIDER; ISSN: 1354-3784

PUBLISHER: Informa Healthcare

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Background: Dopamine replacement therapies (levodopa, dopamine receptor agonists, anticholinergics, monoamine oxidase B inhibitors, and catechol-O-methyltransferase inhibitors) remain the cornerstones of therapeutic interventions for Parkinson's disease (PD). Despite the treatment options for PD symptoms, a cure remains elusive. An optimal treatment would be one that combined relief in both motor and nonmotor

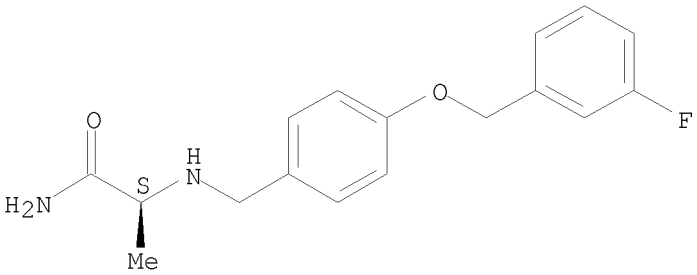
symptoms with neuroprotective properties. Safinamide is an investigational drug for PD currently in development as add-on therapy to both dopamine agonists and levodopa. Safinamide is a unique mol. with a novel mode of action, targeting both dopaminergic and glutaminergic systems, and potentially provides motor symptom control. Preliminary results from exptl. models suggest potential neuroprotective effects. Studies on the potential effects on nonmotor symptoms are ongoing. Objective: To review the mechanism of action and pharmacokinetics, and to evaluate the available clin. safety and efficacy results of safinamide. Methods: A search of the electronic database MEDLINE (PubMed, no time limits) was performed on 14 Dec. 2007. The full text of all citations was obtained for review. Furthermore, two abstrs. on safinamide published as proceedings of a European conference were reviewed. Results/conclusion: Safinamide is a promising investigational drug for PD with a novel mode of action. Early reports confirm the potential efficacy of safinamide in PD. Further studies on potential effects on cognition and neuroprotection are needed.

IT 133865-89-1, Safinamide
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(safinamide in treatment Parkinson's disease)

RN 133865-89-1 CAPLUS

CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:29459 CAPLUS

DOCUMENT NUMBER: 148:345134

TITLE: Monoamine oxidase-B inhibition in the treatment of Parkinson's disease

AUTHOR(S): Fernandez, Hubert H.; Chen, Jack J.

CORPORATE SOURCE: Movement Disorders Center, McKnight Brain Institute, University of Florida, Gainesville, FL, USA

SOURCE: Pharmacotherapy (2007), 27(12, Pt. 2), 174S-185S
CODEN: PHPYDQ; ISSN: 0277-0008

PUBLISHER: Pharmacotherapy Publications

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Inhibitors of monoamine oxidase (MAO) with selectivity and specificity for MAO type B prolong the activity of both endogenously and exogenously derived dopamine, making them an option either as monotherapy in early Parkinson's disease or as adjunctive therapy in patients treated with levodopa who are experiencing motor complications. In addition to symptomatic benefits, exptl. data suggest that MAO-B

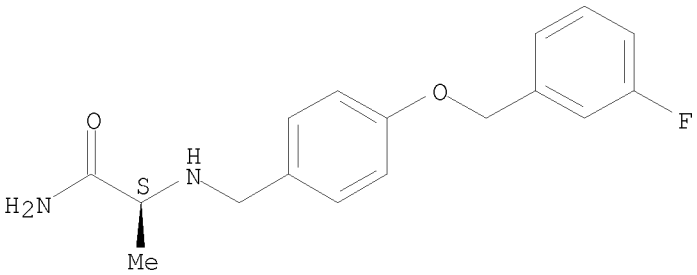
inhibitors may be neuroprotective through MAO-B inhibition and other mechanisms that have yet to be clearly defined. The two available MAO-B inhibitors approved for use in the United States, rasagiline and selegiline, each provide symptomatic relief as monotherapy and as adjunctive therapy, and have shown potential disease-modifying effects in exptl. models and clin. studies. Selegiline in a conventional tablet formulation is less bioavailable than rasagiline, resulting in limited potency. It also has amphetamine metabolites that may produce adverse effects and interfere with any putative disease-modifying effects. The oral disintegrating tablet formulation of selegiline allows pregastric absorption, minimizing first-pass metabolism, thereby increasing selegiline bioavailability and reducing the concentration of amphetamine metabolites. Rasagiline, more potent than selegiline, exhibits disease-modifying effects in exptl. models and lacks amphetamine metabolites. Both the symptomatic and potential disease-modifying effects of rasagiline are under investigation. A third agent with MAO-B inhibition properties, safinamide, is in phase III development. Although not yet approved, safinamide may offer the added advantage of combined MAO-B and dopamine reuptake inhibition.

IT 133865-89-1, Safinamide
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoamine oxidase-B inhibition in treatment of Parkinson's disease)

RN 133865-89-1 CAPLUS

CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 92 THERE ARE 92 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2007:1469897 CAPLUS

DOCUMENT NUMBER: 148:100890

TITLE: Process for the production of 2-[4-(3- and 2-fluorobenzyloxy)benzylamino]propanamides (safinamide and ralfinamide) of high purity by catalytic hydrogenation of Schiff base intermediates and their use for treating CNS disorders

INVENTOR(S): Barbanti, Elena; Caccia, Carla; Salvati, Patricia; Velardi, Francesco; Rufilli, Tiziano; Bogogna, Luigi

PATENT ASSIGNEE(S): Newron Pharmaceuticals S.p.A., Italy

SOURCE: PCT Int. Appl., 77pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007147491	A1	20071227	WO 2007-EP5105	20070608
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2007263328	A1	20071227	AU 2007-263328	20070608
AU 2007263328	A2	20090219		
CA 2653012	A1	20071227	CA 2007-2653012	20070608
EP 2029524	A1	20090304	EP 2007-764601	20070608
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				
MX 2008015704	A	20090109	MX 2008-15704	20081209
US 20090156678	A1	20090618	US 2008-338825	20081218
CN 101472880	A	20090701	CN 2007-80022879	20081219
NO 2009000231	A	20090116	NO 2009-231	20090114
KR 2009021392	A	20090303	KR 2009-701124	20090119
IN 2009CN00339	A	20090605	IN 2009-CN339	20090119
PRIORITY APPLN. INFO.:			EP 2006-12565 A	20060619
			WO 2007-EP5105 W	20070608

OTHER SOURCE(S): CASREACT 148:100890; MARPAT 148:100890
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is related to a process for preparation of therapeutically active 2-[4-(3- and 2-fluorobenzyloxy)benzylamino]propanamides I (safinamide (3-F) and ralfinamide (2-F)) and their pharmaceutically acceptable salts with high purity, in particular, with a content of dibenzyl derivative impurities II <0.03 weight %, preferably <0.01 weight %, via catalytic hydrogenation of the corresponding Schiff base intermediates III in the presence of a heterogeneous catalyst in a protic organic solvent. For example, α-aminoamides I and their pharmaceutically acceptable salts were prepared by fluorobenzylation of hydroxybenzaldehydes with fluorobenzyl derivs. IV [Y = Cl, Br, I, OSO2Me, OSO2c6H4-p-Me] using phase transfer catalysts, iminoalkylation of the benzaldehydes with L-alaninamide in a protic organic solvent, catalytic hydrogenation of Schiff base intermediates III in the presence of a heterogeneous catalyst in a protic organic solvent and acidulation of I with a pharmaceutically acceptable acid. Thus, fluorobenzylation of 4-hydroxybenzaldehyde with 2-fluorobenzyl chloride in toluene in the presence of potassium carbonate and tetradecyltrimethylammonium bromide gave 4-[(2-fluorobenzyl)oxy]benzaldehyde (V) which was recrystd. from diisopropyl ether gave V and a content of 3-(2-fluorobenzyl)-4-[(2-fluorobenzyl)oxy]benzaldehyde of 0.005 weight %. Iminoalkylation of fluorobenzyloxybenzaldehyde V with L-alaninamide

hydrochloride in MeOH in the presence of TEA gave Schiff base III (2-F) which was hydrogenated in the presence of wet (50% H2O) Pt/C at 5 bars and 35° gave ralfinamide in 93% yield with a a content of (S)-2-[[3-(2-fluorobenzyl)-4-[(2-fluorobenzyl)oxy]benzyl]amino]propanamide of 0.02 weight %. Ralfinamide methanesulfonate (preparation given) containing 0.05 % dibenzylated impurity II (2-F) was tested in a cytotoxicity assay in human neuroblastoma cell line SH-SY-5Y, in a HERG current inhibition assay in transfected CHO cell lines and in a maximal electroshock test in mice and compared to II and to methanesulfonate containing II 0.3 %. As the amount of II present in ralfinamide increases, so do the undesirable features, such as cellular toxicity, strong inhibition of Cytochrome P 450, HERG channel blockage, and no protective activity in the in vivo model of epilepsy.

IT 202825-46-5P
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); PUR (Purification or recovery); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of safinamide and ralfinamide and their salts from hydroxybenzaldehydes by fluorobenzylation, iminoalkylation and catalytic hydrogenation)

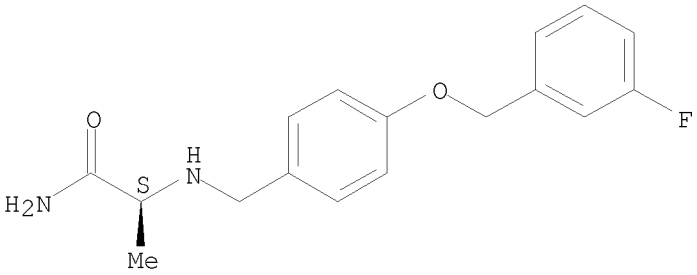
RN 202825-46-5 CAPLUS

CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

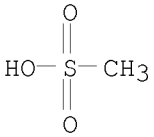
CRN 133865-89-1
CMF C17 H19 F N2 O2

Absolute stereochemistry. Rotation (+).



CM 2

CRN 75-75-2
CMF C H4 O3 S



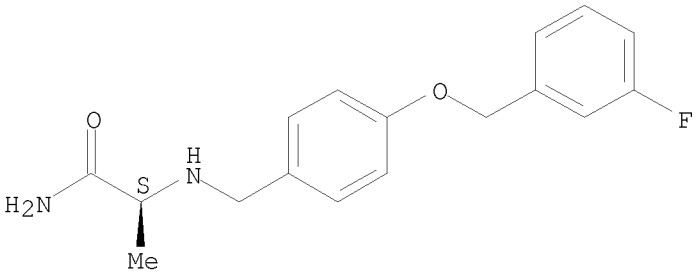
IT 133865-89-1P, Safinamide
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); PUR (Purification or recovery); RCT (Reactant); THU (Therapeutic use); BIOL

(Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of safinamide and ralfinamide from hydroxybenzaldehydes by fluorobenzylation, iminoalkylation and catalytic hydrogenation)

RN 133865-89-1 CAPLUS

CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2007:1454651 CAPLUS

DOCUMENT NUMBER: 148:45877

TITLE: Alpha-aminoamide derivatives useful in the treatment of cognitive disorders

INVENTOR(S): Salvati, Patricia; Rossetti, Stefano; Benatti, Luca

PATENT ASSIGNEE(S): Newron Pharmaceuticals S.p.A., Italy

SOURCE: PCT Int. Appl., 38pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007144153	A2	20071221	WO 2007-EP5197	20070613
WO 2007144153	A3	20080313		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
EP 1870097	A1	20071226	EP 2006-12352	20060615
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
AU 2007260239	A1	20071221	AU 2007-260239	20070613

CA 2655243	A1	20071221	CA 2007-2655243		20070613
EP 2029130	A2	20090304	EP 2007-725989		20070613
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS					
MX 2008016017	A	20090116	MX 2008-16017		20081212
KR 2009018817	A	20090223	KR 2008-730389		20081212
IN 2008KN05055	A	20090327	IN 2008-KN5055		20081212
CN 101466366	A	20090624	CN 2007-80021897		20081212
PRIORITY APPLN. INFO.:			EP 2006-12352	A	20060615
			WO 2007-EP5197	W	20070613

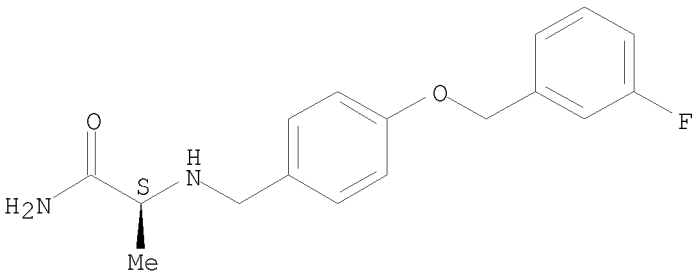
OTHER SOURCE(S): MARPAT 148:45877

AB The present invention is in the field of pharmacotherapy of cognitive deficits in learning and memory by administering an α-aminoamide, particularly safinamide. Examples of disturbances in cognition that can be treated with compds. of the invention are the ones associated with disorders such as autism, dyslexia, attention deficit hyperactivity disorder, schizophrenia, obsessive compulsive disorders, psychosis, bipolar disorders, depression, Tourette's syndrome, Mild Cognitive Impairment (MCI) and disorders of learning in children, adolescents and adults, Age Associated Memory Impairment, Age Associated Cognitive Decline, Alzheimer's Disease, Parkinson's Disease, Down's Syndrome, traumatic brain injury Huntington's Disease, Progressive Supranuclear Palsy (PSP), HIV, stroke, vascular diseases, Pick's or Creutzfeldt- Jakob diseases, multiple sclerosis (MS), other white matter disorders and drug-induced cognitive worsening.

IT 133865-89-1, Safinamide 202825-46-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α-aminoamide derivs. useful in treatment of cognitive disorders)

RN 133865-89-1 CAPLUS
CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

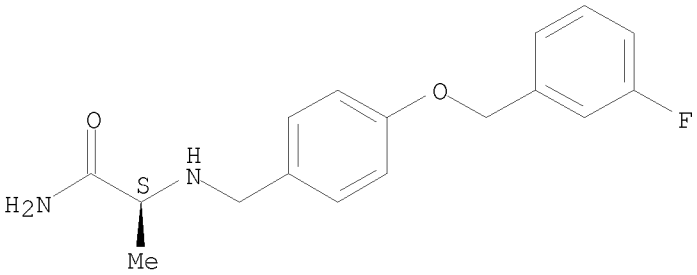


RN 202825-46-5 CAPLUS
CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

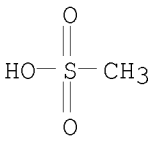
CRN 133865-89-1
CMF C17 H19 F N2 O2

Absolute stereochemistry. Rotation (+).



CM 2

CRN 75-75-2
CMF C H4 O3 S



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L3 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:1088890 CAPLUS
DOCUMENT NUMBER: 147:392440
TITLE: Transdermal delivery of systemically active central nervous system drugs
INVENTOR(S): Carrara, Dario Norberto R.; Grenier, Arnaud; Alberti, Igno; Henry, Laetitia; Decaudin, Celine
PATENT ASSIGNEE(S): Switz.
SOURCE: U.S. Pat. Appl. Publ., 24pp., Cont.-in-part of U.S. Ser. No. 634,005.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20070225379	A1	20070927	US 2007-755923	20070531
WO 2002011768	A1	20020214	WO 2001-EP9007	20010803
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20030199426	A1	20031023	US 2003-343570	20030519
US 7214381	B2	20070508		
AU 2004283431	A1	20050506	AU 2004-283431	20041006

CA 2538856	A1	20050506	CA 2004-2538856		20041006
WO 2005039531	A1	20050506	WO 2004-EP11175		20041006
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
EP 1670433	A1	20060621	EP 2004-790156		20041006
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK					
BR 2004014551	A	20061031	BR 2004-14551		20041006
JP 2007508261	T	20070405	JP 2006-530107		20041006
NZ 546106	A	20081031	NZ 2004-546106		20041006
US 20060153905	A1	20060713	US 2006-371042		20060307
US 7335379	B2	20080226			
ZA 2006002046	A	20070627	ZA 2006-2046		20060310
MX 2006003316	A	20060608	MX 2006-3316		20060324
US 20070098775	A1	20070503	US 2006-634005		20061204
US 7404965	B2	20080729			
US 20090069364	A1	20090312	US 2008-268301		20081110
PRIORITY APPLN. INFO.:			WO 2001-EP9007	W	20010803
			US 2003-343570	A1	20030519
			US 2003-510613P	P	20031010
			WO 2004-EP11175	A1	20041006
			US 2006-371042	A2	20060307
			US 2006-634005	A2	20061204
			WO 2000-EP7533	A	20000803
			US 2007-755923	A2	20070531

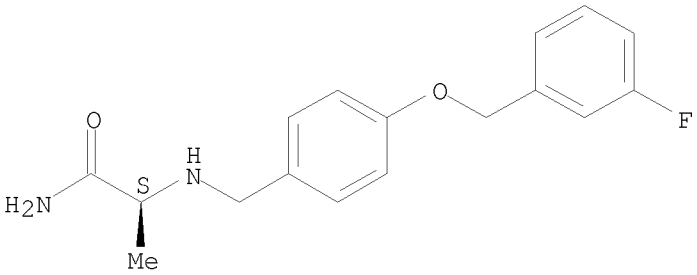
AB The invention relates to a transdermal or transmucosal non-occlusive, semi-solid pharmaceutical formulation that includes at least one systemically active agent that acts on the central nervous system (CNS) of a mammal; and a permeation enhancing solvent system present in an amount sufficient to solubilize the at least one active ingredient. The permeation enhancing solvent system includes a pharmaceutically acceptable monoalkyl ether of diethylene glycol; a pharmaceutically acceptable glycol; preferably also a fatty alc. and or a fatty acid; and a mixture of a C2 to C4 alc. and water so that the permeation enhancing solvent system (a) inhibits crystallization of the at least one active ingredient on a skin or mucosal surface of a mammal, (b) reduces or prevents transfer of the formulation to clothing or to another being, (c) modulates biodistribution of the at least one active agent within different layers of skin, (d) facilitates absorption of the at least one active agent by a skin or a mucosal surface of a mammal, or (e) provides a combination of one or more of (a) through (d). A transdermal pharmaceutical contained pramipexole dihydrochloride 2.00, diethylene glycol monoethyl ether 5.00, propylene glycol 15.0, hydroxypropylcellulose 1.50, absolute ethanol 4.0, sodium hydroxide q.s. pH = 8.2, and water q.s. 100.00%.

IT 133865-89-1, Safinamide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transdermal delivery of systemically active central nervous system drugs)

RN 133865-89-1 CAPLUS

CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

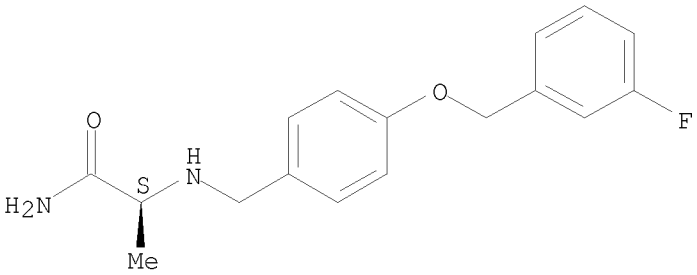
Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

L3 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:997166 CAPLUS
DOCUMENT NUMBER: 147:502595
TITLE: Solid-Phase Synthesis and Insights into Structure-Activity Relationships of Safinamide Analogues as Potent and Selective Inhibitors of Type B Monoamine Oxidase
AUTHOR(S): Leonetti, Francesco; Capaldi, Carmelida; Pisani, Leonardo; Nicolotti, Orazio; Muncipinto, Giovanni; Stefanachi, Angela; Cellamare, Saverio; Caccia, Carla; Carotti, Angelo
CORPORATE SOURCE: Dipartimento Farmaco-Chimico, University of Bari, Bari, I-70125, Italy
SOURCE: Journal of Medicinal Chemistry (2007), 50(20), 4909-4916
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 147:502595
AB Safinamide, an anti-Parkinson drug in phase III clin. trials, and its alkanamidic analogs were prepared via expeditious solid-phase synthesis and evaluated for their monoamine oxidase B (MAO-B) and monoamine oxidase A (MAO-A) inhibitory activity and selectivity. (S)-3-Chlorobenzyloxyalaninamide (8) and (S)-3-chlorobenzyloxyserinamide (13) derivs. proved to be more potent MAO-B inhibitors than safinamide (IC50 = 33 and 43 nM, resp., vs. 98 nM) but with a lower MAO-B selectivity (SI = 3455 and 1967, resp., vs. 5918). The highest MAO-B inhibitory potency (IC50 = 17 nM) and a good selectivity (SI = 2941) were displayed by (R)-2-[6-(3-fluorobenzyloxy)-3,4-dihydro-1H-isoquinolin-2-yl]propionamide (R-21), a tetrahydroisoquinoline analog of safinamide. Structure-affinity relationships and docking simulations pointed out strong neg. steric effects of α-amino acid amide side chains and para substituents of the benzyloxy groups and favorable hydrophobic interactions of meta substituents. The significantly diverse MAO-B affinities of a number of (R)- and (S)-α-amino acid amide enantiomers, including the two rigid analogs (21) of safinamide, indicated likely enantioselective interactions at the enzymic binding sites.
IT 133865-89-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(solid-phase preparation and structure-activity relationships of safinamide and its analogs as inhibitors of type B monoamine oxidase)
RN 133865-89-1 CAPLUS
CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

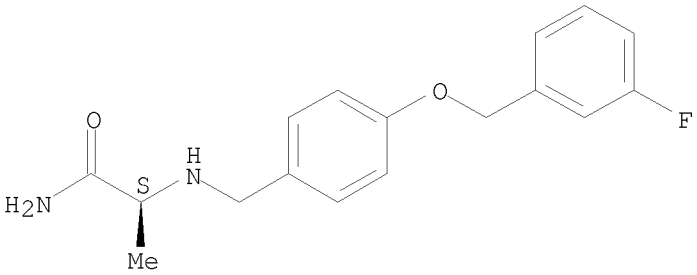
Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:926416 CAPLUS
DOCUMENT NUMBER: 147:356131
TITLE: Drug evaluation: safinamide for the treatment of Parkinson's disease, epilepsy and restless legs syndrome
AUTHOR(S): Chazot, Paul L.
CORPORATE SOURCE: Centre for Integrative Neuroscience (CINS) School of Biological and Biomedical Sciences, Durham University, Durham, DH1 3LE, UK
SOURCE: Current Opinion in Investigational Drugs (Thomson Scientific) (2007), 8(7), 570-579
CODEN: COIDAZ; ISSN: 1472-4472
PUBLISHER: Thomson Scientific
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Merck Serono SA (formerly Serono), under license from Newron Pharmaceuticals SpA (following its acquisition of the rights from Pharmacia and Upjohn AB [now Pfizer Inc]), is developing the oral α-aminoamide derivative of milacemide, safinamide, a monoamine oxidase-B and glutamate release inhibitor, for the potential treatment of Parkinson's disease, epilepsy and restless legs syndrome. In March 2007, plans to develop the agent for the potential treatment of other cognitive disorders, such as Alzheimer's disease, were being finalized and testing was expected to begin before the end of that year.
IT 133865-89-1, Safinamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Merck Serono SA under license from Newron Pharmaceuticals SpA is developing safinamide for potential treatment of Parkinson's disease, epilepsy and restless legs syndrome in human)
RN 133865-89-1 CAPLUS
CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

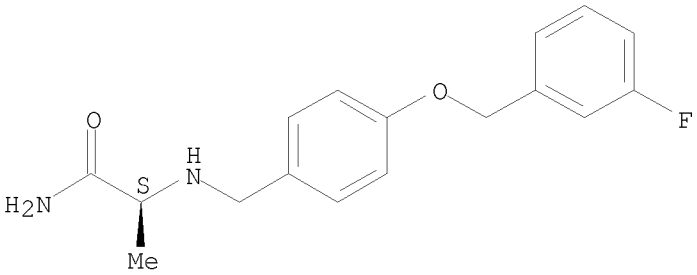
L3 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:252730 CAPLUS
DOCUMENT NUMBER: 146:371665
TITLE: Safinamide
AUTHOR(S): Fariello, Ruggero G.
CORPORATE SOURCE: BioNeuroFar s.a.s, Luino, Italy
SOURCE: Neurotherapeutics (2007), 4(1), 110-116
CODEN: NEURNV; ISSN: 1933-7213
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Safinamide (SAF) ((S)-(+)-2-(4-(3-fluorobenzyloxy) benzylamino)propanamide) was initially synthesized by Farmitalia Carlo Erba (Italy). Following initial anticonvulsant screening, safinamide was selected for its potency, broad spectrum of action, and good safety margin. Pharmacodynamic properties probably relevant to its antiepileptic activity are use- and frequency-dependent block of voltage sensitive Na+ channels, block of Ca++ channels, and glutamate release inhibition. Possibly contributing mechanism are also selective and reversible monoamide oxidase B inhibition and dopamine and noradrenaline uptake inhibition. The high selectivity for the sigma-1 receptor site does not entail psychotomimetic or behavioral changes. In several exptl. in vitro and in vivo conditions, SAF exerts neurorescuing and neuroprotectant effects. Safinamide is water soluble and suitable for 1 times a day oral administration in humans. In a pilot phase II study in 38 refractory epilepsy patients affected by multiple types of seizures, 41% of subjects obtained ≥50% seizure reduction during a 12-wk escalating dose up to 300 mg 1 times day compared with perspective baseline. Safinamide is being developed in phase III for treatment of Parkinson's disease, whereas the development in epilepsy relates to the industrial strategy of the company.

IT 133865-89-1, Safinamide
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetics and pharmacodynamic anal. showed safinamide exhibited anticonvulsant activity with neurorescuing and neuroprotectant effects in refractory epilepsy patient)

RN 133865-89-1 CAPLUS
CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:1039299 CAPLUS
DOCUMENT NUMBER: 147:22182
TITLE: New pharmacologic horizons in the treatment of Parkinson disease
AUTHOR(S): Bonuccelli, Ubaldo; Del Dotto, Paolo
CORPORATE SOURCE: Department of Neurocience, University of Pisa and Neurology Unit, Pisa, Italy
SOURCE: Neurology (2006), 67(7, Suppl. 2), S30-S38
CODEN: NEURAI; ISSN: 0028-3878
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Many of the motoric features that define Parkinson's disease (PD) result primarily from the loss of dopaminergic neurons of the substantia nigra. l-dopa remains at present the most powerful symptomatic drug for the treatment of this condition. However, motor complications of chronic l-dopa treatment have emerged as a major limitation of this therapy. Slowing or delaying the progression of the disease with neuroprotective therapies may delay the need for l-dopa. In the past few years, novel insight into the pathogenetic mechanisms of neurodegeneration in PD has been provided. Mitochondrial function deficiency, increased oxidative stress, apoptosis, excitotoxicity, and inflammation are part of the processes that ultimately result in neurodegeneration. Drugs that are now under clin. scrutiny as neuroprotectant include mols. that combine one or more of the following properties: (1) monoamine oxidase inhibition (rasagiline, safinamide); (2) mitochondrial enhancement (coenzyme Q10, creatine); (3) antiapoptotic activity; (4) anti-inflammatory activity; (5) protein aggregation inhibition; (6) neurotrophic activity. In advanced Parkinson's disease, the combination of disease progression and l-dopa therapy leads to the development of motor response complications, particularly wearing off, on off, dyskinesias and dystonias. The nonphysiol. pulsatile stimulation of striatal dopamine receptors, produced by the currently available dopaminergic drugs, may trigger a dysregulation of many neurotransmitter systems within the basal ganglia, mainly localized on medium spiny striatal neurons. These include alterations of glutamatergic, serotonergic, adrenergic and adenosine A2A receptors. Novel strategies for pharmacol. intervention with nondopaminergic treatments hold the promise of providing effective control or reversal of motor response complications. Of particular interest are NMDA and AMPA antagonists or drugs acting on 5-HT subtype 2A, alpha2-adrenergic, and adenosine A2 receptors. Future strategies may also target pre- and postsynaptic components that regulate firing pattern of basal ganglia neurons, such as synaptic vesicle proteins, nonsynaptic gap junction

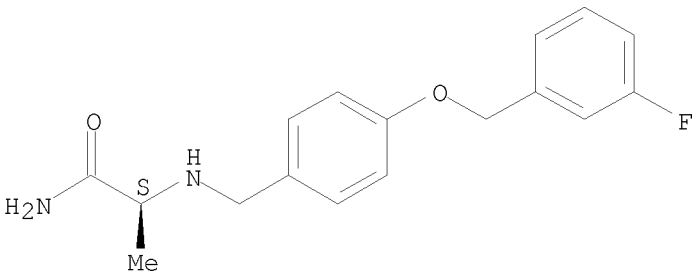
communication mechanisms, or signal transduction systems that modulate the phosphorylation state of glutamatergic receptors.

IT 133865-89-1, Safinamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(safinamide inhibited monoamine oxidase in patient with Parkinson's disease)

RN 133865-89-1 CAPLUS

CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)

REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:1039298 CAPLUS

DOCUMENT NUMBER: 147:23401

TITLE: Symptom relief in Parkinson disease by safinamide: Biochemical and clinical evidence of efficacy beyond MAO-B inhibition

AUTHOR(S): Stocchi, F.; Vacca, L.; Grassini, P.; De Pandis, M. F.; Battaglia, G.; Cattaneo, C.; Fariello, R. G.

CORPORATE SOURCE: IRCCS San Raffaele Pisana, Rome, Italy

SOURCE: Neurology (2006), 67(7, Suppl. 2), S24-S29
CODEN: NEURAI; ISSN: 0028-3878

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In an open pilot study, doses of safinamide (100, 150, and 200 mg once a day, higher than previously tested) were administered to 13 parkinsonian patients along with a stable dose of dopamine (DA) agonist, causing a significant progressive improvement in motor performance as evaluated by the Unified Parkinson Disease Rating Scale (UPDRS) part III over an 8-wk period (4.2 points; $P < 0.001$). In association with levodopa, the same doses of safinamide in another group of patients (N = 11) induced a significant decrease in motor fluctuations (UPDRS part IV, 2.1 points; $P < 0.001$), accompanied by a dose-proportional increase of the levodopa AUC, up to 77% from baseline. Because MAO-B was fully inhibited (95%) at all doses tested, we suggest that these biochem. and symptomatic dose-dependent effects must be related to addnl. mechanisms of action, such as inhibition of glutamate release, increased dopamine release, or inhibition of dopamine re-uptake. These hypotheses are under investigation and will pursue confirmation in controlled clin. trials.

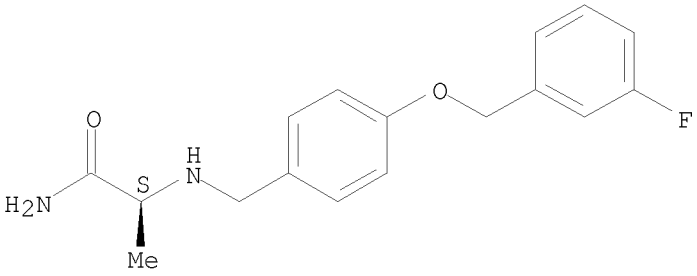
IT 133865-89-1, Safinamide
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy of safinamide and levodopa lowered motor fluctuations showing symptom relief while inhibited glutamate release or dopamine reuptake and raised dopamine release due to MAO-B inhibition in patient with Parkinson's disease)

RN 133865-89-1 CAPLUS

CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 17 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:1039297 CAPLUS

DOCUMENT NUMBER: 147:22181

TITLE: Safinamide: From molecular targets to a new anti-Parkinson drug

AUTHOR(S): Caccia, C.; Maj, R.; Calabresi, M.; Maestroni, S.; Faravelli, L.; Curatolo, L.; Salvati, P.; Fariello, R. G.

CORPORATE SOURCE: Newron Pharmaceuticals Spa, Bresso, Italy

SOURCE: Neurology (2006), 67(7, Suppl. 2), S18-S23
CODEN: NEURAI; ISSN: 0028-3878

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Ideal treatment in Parkinson's disease (PD) aims at relieving symptoms and slowing disease progression. Of all remedies, levodopa remains the most effective for symptomatic relief, but the medical need for neuroprotectant drugs is still unfulfilled. Safinamide, currently in phase III clin. trials for the treatment of PD, is a unique mol. with multiple mechanisms of action and a very high therapeutic index. It combines potent, selective, and reversible inhibition of MAO-B with blockade of voltage-dependent Na and Ca channels and inhibition of glutamate release. Safinamide has neuroprotective and neuro rescuing effects in MPTP-treated mice, in the rat kainic acid, and in the gerbil ischemia model. Safinamide potentiates levodopa-mediated increase of DA levels in DA-depleted mice and reverses the waning motor response after prolonged levodopa treatment in 6-OHDA-lesioned rats. Safinamide has excellent bioavailability, linear kinetics, and is suitable for once-a-day administration. Therefore, safinamide may be used in PD to reduce l-dopa dosage and also represents a valuable therapeutic drug to test disease-modifying potential.

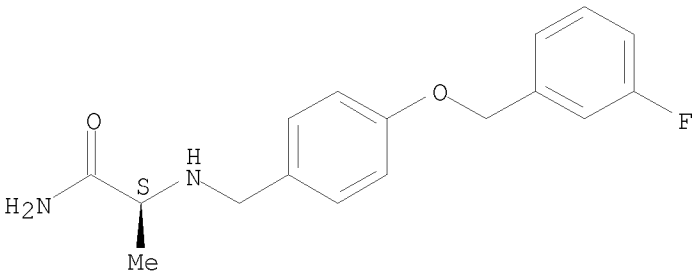
IT 133865-89-1, Safinamide
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(safinamide had neuroprotective and neurorescuing effects in mouse, rat and gerbil ischemia model, suggests that safinamide may be used in Parkinson's disease patient to reduce levodopa dosage)

RN 133865-89-1 CAPLUS

CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:215887 CAPLUS

DOCUMENT NUMBER: 142:285193

TITLE: medicinal compositions containing adenosine A2A receptor antagonists and dopamine agonists

INVENTOR(S): Kase, Hiroshi; Kobayashi, Minoru; Shiozaki, Shizuo; Mori, Akihisa; Senoo, Naoki

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 22 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2005060370	A	20050310	JP 2004-215147	20040723
PRIORITY APPLN. INFO.:			JP 2003-201548 A	20030725

AB The invention provides a pharmaceutical composition characterized by containing an adenosine A2A receptor antagonist (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purin-2 ,6-dione (I) and dopamine agonist, e.g. pramipexole, pergolide mesylate, ropinirole hydrochloride, cabergoline, selegiline hydrochloride, safinamide mesylate, entacapone, and tolcapone, for administering together or separatory for treatment of Parkinson's disease and restless legs syndrome, etc. The effect of combination of I and pramipexole on haloperidol-induced catalepsy in mice was examined

IT 202825-46-5, Safinamide mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicinal compns. containing adenosine A2A receptor antagonists and dopamine agonists)

RN 202825-46-5 CAPLUS

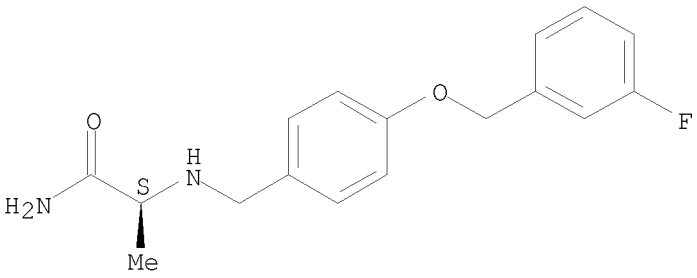
CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)-,

methanesulfonate (1:1) (CA INDEX NAME)

CM 1

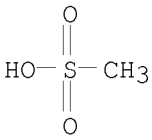
CRN 133865-89-1
CMF C17 H19 F N2 O2

Absolute stereochemistry. Rotation (+).



CM 2

CRN 75-75-2
CMF C H4 O3 S



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L3 ANSWER 19 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:872683 CAPLUS
DOCUMENT NUMBER: 141:370536
TITLE: Combination chemotherapy for treatment of parkinson's disease by using safinamides and MAO-B inhibitors together with other antiparkinsonian agents
INVENTOR(S): Ruggero, Fariello; Cattaneo, Carlo; Salvati, Patricia; Benatti, Luca
PATENT ASSIGNEE(S): Newron Pharmaceuticals, Inc., Italy
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089353	A2	20041021	WO 2004-IB1408	20040408
WO 2004089353	A3	20041216		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2004228782	A1	20041021	AU 2004-228782		20040408
CA 2523188	A1	20041021	CA 2004-2523188		20040408
EP 1613296	A2	20060111	EP 2004-726590		20040408
EP 1613296	B1	20090701			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR					
BR 2004009364	A	20060425	BR 2004-9364		20040408
CN 1771030	A	20060510	CN 2004-80009655		20040408
JP 2006522800	T	20061005	JP 2006-506582		20040408
NZ 542910	A	20071026	NZ 2004-542910		20040408
RU 2342929	C2	20090110	RU 2005-131422		20040408
EP 2070526	A1	20090617	EP 2009-154864		20040408
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR					
AT 435012	T	20090715	AT 2004-726590		20040408
NO 2005004640	A	20051209	NO 2005-4640		20051010
MX 2005010873	A	20060321	MX 2005-10873		20051010
IN 2005DN04581	A	20070817	IN 2005-DN4581		20051010
US 20070093495	A1	20070426	US 2005-559982		20051209
PRIORITY APPLN. INFO.:			US 2003-462205P	P	20030411
			EP 2004-726590	A3	20040408
			WO 2004-IB1408	W	20040408

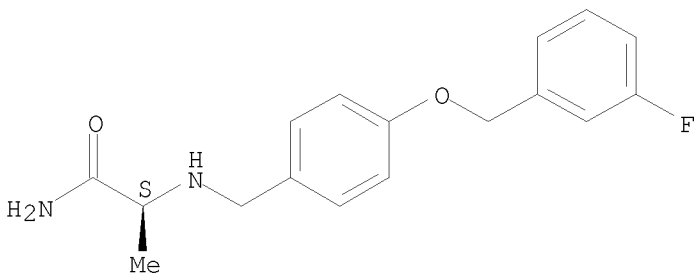
AB New uses of safinamide, safinamide derivs. and MAO-B inhibitors in novel types of treatment for Parkinson's Disease are described. More specifically, the invention relates to methods for treating Parkinson's Disease through the administration of safinamide, a safinamide derivative, or a MAO-B inhibitor, in combination with other Parkinson's Disease agents or treatments, such as levodopa/PDI or dopamine agonists. For example, safinamide as an anticonvulsant was proved through clin. trials to be potent and safe to treat idiopathic early Parkinson's disease.

IT 133865-89-1, Safinamide
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination chemotherapy for treatment of parkinson's disease by using safinamides and MAO-B inhibitors together with dopamine agonists)

RN 133865-89-1 CAPLUS

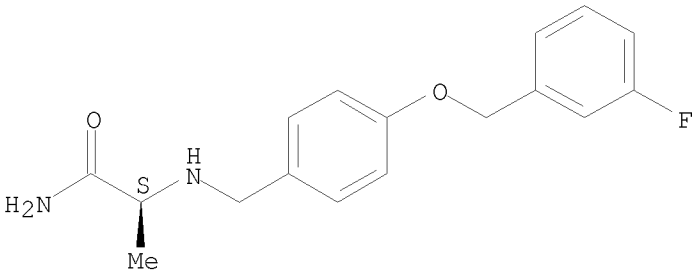
CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 133865-89-1D, Safinamide, derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination chemotherapy for treatment of parkinson's disease by using safinamides and MAO-B inhibitors together with dopamine agonists)
RN 133865-89-1 CAPLUS
CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

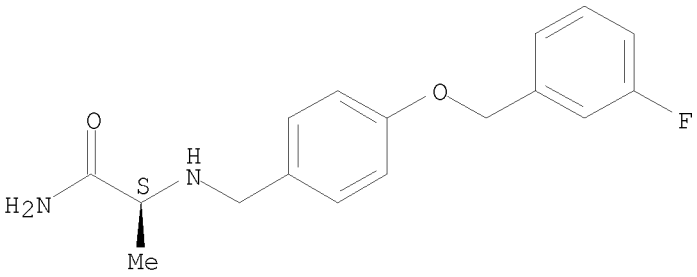


OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:630035 CAPLUS
DOCUMENT NUMBER: 142:169731
TITLE: Improvement of motor function in early Parkinson disease by safinamide
AUTHOR(S): Stocchi, F.; Arnold, G.; Onofrj, M.; Kwiecinski, H.; Szczudlik, A.; Thomas, A.; Bonuccelli, U.; Van Dijk, A.; Cattaneo, C.; Sala, P.; Fariello, R. G.
CORPORATE SOURCE: Safinamide Parkinson's Study Group, Department of Neuroscience and IRCCS Neuromed Pozzilli, University of Pisa, Milan, Italy
SOURCE: Neurology (2004), 63(4), 746-748
CODEN: NEURAI; ISSN: 0028-3878
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A median safinamide (SAF) dose of 70 mg/day (range 40 to 90 mg/day) increased the percentage of parkinsonian patients improving their motor scores by ≥30% from baseline (responders) after 3 mo from 21.4% (placebo) to 37.5% ($p < 0.05$, calculated by logistic regression anal.). In a subgroup of 101 patients under stable treatment with a single dopamine agonist, addition of SAF magnified the response (47.1% responders, mean 4.7-point motor score decrease; $p \geq 0.05$). These results suggest that doses of SAF exerting ion channel block and glutamate release inhibition add to its symptomatic effect and warrant exploration of higher doses.
IT 133865-89-1, Safinamide
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low dose safinamide was well tolerated and increased improvement of motor activity, combination with dopamine agonist magnified response of Parkinson disease patient)
RN 133865-89-1 CAPLUS

CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:304312 CAPLUS
DOCUMENT NUMBER: 141:388094
TITLE: Pharmacokinetics and pharmacodynamics of safinamide, a neuroprotectant with antiparkinsonian and anticonvulsant activity
AUTHOR(S): Marzo, Antonio; Dal Bo, Lorenzo; Monti, Nunzia Ceppi; Crivelli, Fabrizio; Ismaili, Shevqet; Caccia, Carla; Cattaneo, Carlo; Fariello, Ruggero G.
CORPORATE SOURCE: IPAS SA, Ligornetto, 6853, Switz.
SOURCE: Pharmacological Research (2004), 50(1), 77-85
CODEN: PHMREP; ISSN: 1043-6618
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Objective: This paper describes the pharmacokinetics and the pharmacodynamics, in terms of monoamino oxidase type B (MAO-B) inhibition, in male healthy volunteers of orally administered safinamide, a new neuroprotectant that in exptl. models has demonstrated strong anticonvulsant and antiparkinson activities. Methods: Four clin. trials covering the dose range of 25-10,000 μg/kg were carried out to describe pharmacokinetics, pharmacodynamics and tolerability of safinamide, administered in single or repeated dose regimen to steady state, including a food interaction trial. All the above trials were carried out after the Ethics Committee's approval and signature of the consent form by the volunteers. In single dose trials blood sampling covered a 24 h-period in pharmacodynamic trials, 48 h-period in pharmacokinetic trials. In the case of repeated dose regimen to steady state a pre-dose sample was drawn on the first six study days, whereas the curve was explored on the 7th study day, prolonging blood sampling over a 48 h-period after the last dosing. Safinamide level was determined in plasma by a very sensitive and specific LC-MS-MS method, with a low limit of quantification of 0.5 ng/mL of plasma. Pharmacokinetic anal. was carried out with non-compartmental method and, in one case, also with the two-compartmental method. Monoamine oxidase activity of both types A and B (MAO-A and MAO-B) was determined in plasma at different times (MAO-B) and correlated to safinamide levels, or in urine (MAO-A). Results: Pharmacokinetics of safinamide proved to be linearly and proportionally related to the administered doses. The absorption of safinamide was rapid with peak plasma concns. ranging from 2 to 4 h. Food prolonged the rate and did not affect the

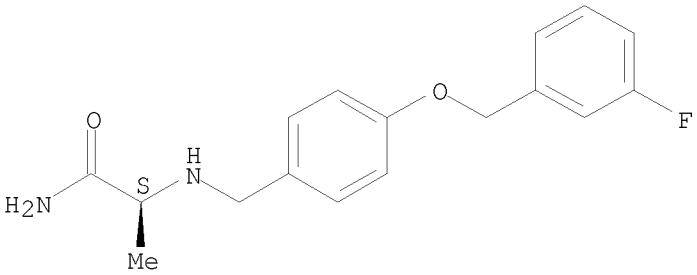
extent of absorption of safinamide. In repeat dose regimen once daily, the steady state was reached on the 5th study day with a marginal accumulation factor of 1.5-1.7. The drug was cleared with a t1/2 of about 22 h. Safinamide reversibly inhibited MAO-B enzyme. Full inhibition was observed with single doses≥600 μg/kg, and a relevant, dose dependent, progressive inhibition was encountered with doses starting from 25 μg/kg. Even at the highest single dose of 10 mg/kg no evidence of MAO-A inhibition was observed Conclusion: Enteral absorption of the drug is linear and proportional to the doses administered. The drug is cleared from the body with a t1/2 of .simeq.22 h, without producing any clin. relevant accumulation at steady state. The MAO-B inhibitory activity, without affecting MAO-A, is useful to prevent a dopamine bioinactivation in patients suffering from Parkinson's disease. Safinamide tolerability in the four clin. trials proved to be good.

IT 133865-89-1, Safinamide
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(pharmacokinetics of safinamide is linear, proportional to doses administered, absorption was rapid and food prolonged rate, did not affect absorption while reversibly inhibited MAO-B enzyme and was well tolerated in human)

RN 133865-89-1 CAPLUS

CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:835216 CAPLUS

DOCUMENT NUMBER: 137:56719

TITLE: Safinamide mesilate Prop INNM NW-1015 PNU-151774E FCE-26743

AUTHOR(S): Sorbera, L. A.; Leeson, P. A.; Castaner, J.

CORPORATE SOURCE: Prous Science, Barcelona, 08080, Spain

SOURCE: Drugs of the Future (2001), 26(8), 745-749
CODEN: DRFUD4; ISSN: 0377-8282

PUBLISHER: Prous Science

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. In an attempt to discover new, potent and safe anticonvulsant agents, a lead compound safinamide mesilate (NW-1015; PNU-151774E) emerged. It has no affinity for GABA receptors or excitatory amino acid receptors but exhibits high affinity for sodium channels and sigma-1 binding sites. Safinamide has also been shown to be a calcium antagonist and monoamine oxidase (MAO)-B and glutamate release inhibitor. Due to its broad spectrum of action demonstrated in vitro and its in vivo anticonvulsant

activity, safinamide was chosen for further development as a treatment for epilepsy and as a potential therapy for motor dysfunction associated with Parkinson's disease.

IT 202825-46-5P, Safinamide mesylate
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(safinamide mesilate for treatment of epilepsy)

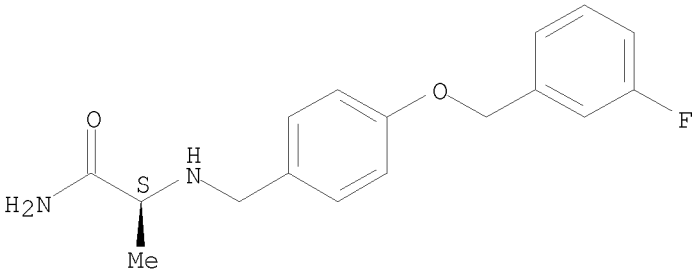
RN 202825-46-5 CAPLUS

CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

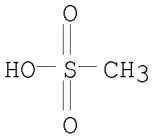
CRN 133865-89-1
CMF C17 H19 F N2 O2

Absolute stereochemistry. Rotation (+).



CM 2

CRN 75-75-2
CMF C H4 O3 S



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:536149 CAPLUS
DOCUMENT NUMBER: 135:312970
TITLE: Safinamide (Newron Pharmaceuticals)
AUTHOR(S): Chazot, Paul L.
CORPORATE SOURCE: School of Sciences, University of Sunderland, Tyne and Wear, SR2 3SD, UK
SOURCE: Current Opinion in Investigational Drugs (PharmaPress Ltd.) (2001), 2(6), 809-813
CODEN: COIDAZ
PUBLISHER: PharmaPress Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with refs. Safinamide (formerly PNU-151774E), a sodium and

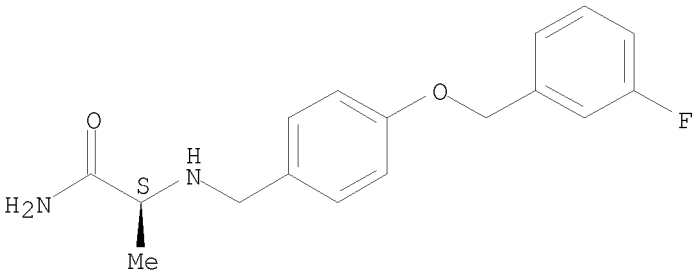
calcium channel modulator that also inhibits monoamine oxidase B (MAOB), is under development by Newron Pharmaceuticals for the potential treatment of epilepsy, Parkinson's disease (PD), pain and stroke. Phase I trials for epilepsy and PD have been completed, and dose-finding studies for both indications had commenced in Mar. 2001. The compound was previously developed by Pharmacia & Upjohn (P&U) for the potential treatment of epilepsy, an indication for which it initially reached phase I trials. Newron acquired the rights to safinamide from P&U at the end of 1998. Results from two phase I trials of the compound (single ascending dose and steady state at three doses), completed in Mar. 2000, demonstrated that the drug is well tolerated with good bioavailability and linear pharmacokinetics.

IT 133865-89-1, Safinamide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(safinamide for potential treatment of epilepsy, Parkinson's disease (PD), pain and stroke in humans)

RN 133865-89-1 CAPLUS

CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 24 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:824917 CAPLUS
DOCUMENT NUMBER: 134:348174
TITLE: Restoration and putative protection in Parkinsonism
AUTHOR(S): Archer, Trevor; Fredriksson, Anders
CORPORATE SOURCE: Department of Psychology, University of Goteborg, Goteborg, S-405 30, Swed.
SOURCE: Neurotoxicity Research (2000), 2(2-3), 251-292
CODEN: NURRFI; ISSN: 1029-8428
PUBLISHER: Harwood Academic Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

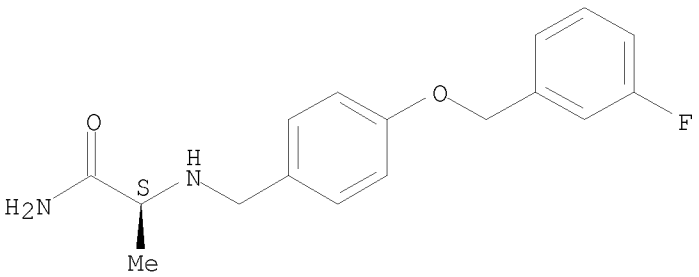
AB Synergistic antiparkinsonian actions of different classes of putative therapeutic agents coadministered with a subthreshold dose of L-dopa (5 mg/kg) in drug-naive, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-treated mice, as well as the restorative actions of those compds. in suprathreshold-L-dopa-tolerant MPTP-treated mice subjected to "wearing-off" of L-dopa efficacy, were assessed. The classes of compds. studied included the noncompetitive NMDA antagonists memantine, amantadine and MK-801, the anticonvulsive and putative anticonvulsive agents

lamotrigine, FCE 26743, and phenytoin, the monoamine oxidase inhibitors L-deprenyl, amiflamine, α-ethyltryptamine, clorgyline and phenelzine, and the α2-adrenoceptor agonists clonidine and guanfacine. The restorative effects of clonidine and guanfacine were antagonized by the α2-adrenoceptor antagonist yohimbine, but not the α1-adrenoceptor antagonist prazosin. Within each class of potentially therapeutic agents a differential restorative efficacy was obtained, but the combination of different doses of apomorphine with clonidine failed to restore motor activity. Finally, the neuroprotective actions of acute and subchronic administration of the nitrone spin-trapping compound α-phenyl-tert-Bu nitrone on the spontaneous motor behavior and striatal dopamine concns. of MPTP-treated mice were examined A considerable amount of review material is also presented in this paper.

IT 133865-89-1, FCE 26743
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(classes of compds. with protective or restorative effect in MPTP model of Parkinsonism in mice)

RN 133865-89-1 CAPLUS
CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 170 THERE ARE 170 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1991:228554 CAPLUS
DOCUMENT NUMBER: 114:228554
ORIGINAL REFERENCE NO.: 114:38536h,38537a
TITLE: Preparation of α-(phenylalkylamino)carboxamides as drugs
INVENTOR(S): Dostert, Philippe; Pevarello, Paolo; Heidempergher, Franco; Varasi, Mario; Bonsignori, Alberto; Roncucci, Romeo
PATENT ASSIGNEE(S): Farmitalia Carlo Erba S.r.l., Italy
SOURCE: Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

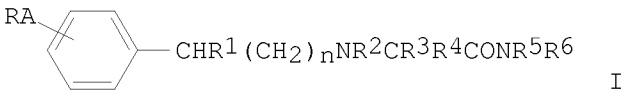
EP 400495	A1	19901205	EP 1990-109950	19900525
EP 400495	B1	19931103		
R: GR				
IL 94466	A	19950124	IL 1990-94466	19900522
ZA 9003990	A	19910327	ZA 1990-3990	19900523
CZ 281420	B6	19960911	CZ 1990-2520	19900523
CA 2033190	A1	19901126	CA 1990-2033190	19900525
CA 2033190	C	20030408		
WO 9014334	A1	19901129	WO 1990-EP841	19900525
W: AU, CA, FI, HU, JP, KR, NO, SU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
CN 1047496	A	19901205	CN 1990-103800	19900525
CN 1027588	C	19950208		
AU 9057299	A	19901218	AU 1990-57299	19900525
AU 645752	B2	19940127		
EP 426816	A1	19910515	EP 1990-908218	19900525
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE				
HU 55348	A2	19910528	HU 1990-5133	19900525
JP 04500215	T	19920116	JP 1990-507938	19900525
JP 2771328	B2	19980702		
AT 96775	T	19931115	AT 1990-109950	19900525
ES 2062174	T3	19941216	ES 1990-109950	19900525
DD 298507	A5	19920227	DD 1990-344386	19901002
NO 9100270	A	19910123	NO 1991-270	19910123
NO 179944	B	19961007		
NO 179944	C	19970115		
US 5236957	A	19930817	US 1991-646596	19910125
RU 2097371	C1	19971127	RU 1992-5011522	19920319
US 5391577	A	19950221	US 1993-65888	19930525
US 5502079	A	19960326	US 1994-343853	19941117

PRIORITY APPLN. INFO.:

GB 1989-12071	A	19890525
GB 1990-7567	A	19900404
EP 1990-109950	A	19900525
WO 1990-EP841	A	19900525
US 1991-646596	A3	19910125
US 1993-65888	A3	19930525

OTHER SOURCE(S): MARPAT 114:228554

GI



I

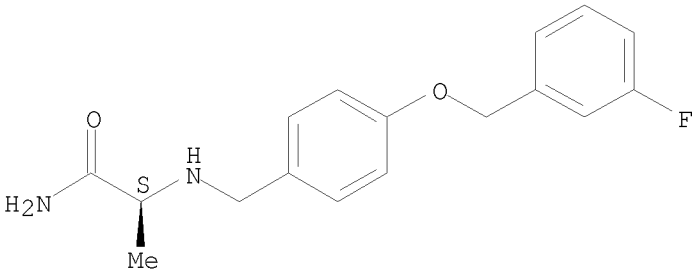
AB Title compds. I [R = C1-8 alkyl, C3-8 cycloalkyl, furyl, thienyl, pyridyl, (substituted) Ph; R1, R2 = H, C1-4 alkyl; R3 = H, (substituted) C1-4 alkyl; R4 = H; R3R4C = C3-6-cycloalkyl; R5, R5 = H, C1-6 alkyl; A = alkyl, (CH2)pX(CH2)q; 1 of p and q is 0 and the other is 0-4; X = O, S, HN, C1-4 alkylimino; n = 0, 1] and salts thereof, are prepared as antiepileptic, anti-Parkinson, neuroprotective, antidepressant, antispastic, and(or) hypnotic agents. H2NCH2CONH2.HCl in MeOH and NaBH3CN were added under N to 4-(3-ClC6H4O)C6H4CHO to give I [RA = 4-(3-ClC6H4); R1-R6 = H; n = 0] as the HCl. (S)-I (RA = 4-PhCH2NH; R1 = R2 = R4 = R5 = R6 = H; R3 = Me; n = 0) similarly prepared showed antagonism of convulsions induced by bicuculline, in mice at ED50 = 9 mg/kg, orally. Tablet formulations comprising I are given.

IT 133865-89-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological

study); PREP (Preparation)
(preparation of, as drug)
RN 133865-89-1 CAPLUS
CN Propanamide, 2-[[[4-[(3-fluorophenyl)methoxy]phenyl]methyl]amino]-, (2S)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 24 THERE ARE 24 CAPLUS RECORDS THAT CITE THIS RECORD (31 CITINGS)

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	144.74	155.33

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-20.50	-20.50

FILE 'STNGUIDE' ENTERED AT 21:46:39 ON 13 SEP 2009
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Sep 11, 2009 (20090911/UP).

=> s l3 and ldopa
0 SAFINAMIDE
1 PARKINSON
0 LDOPA
L4 0 L3 AND LDOPA

=> s L-DOPA
118 L
0 DOPA
L5 0 L-DOPA
(L(W)DOPA)

=> s levadopa
L6 0 LEVADOPA

=> s dopa
DOPA IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s dopa

L7 0 DOPA

=>